Remarks

Claims 1-44 are pending in the subject application. By this Amendment, Applicant has canceled claims 26-44 and added new claims 45-65. Support for the amendments and new claims can be found throughout the subject specification and in the claims as originally filed (see, for example, pages 10-17 and the Examples of the as-filed application). Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1-25 and 45-65 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

Submitted herewith is a supplemental Information Disclosure Statement (IDS), accompanied by the form PTO/SB/08, and a copy of the Perreault *et al.* reference cited herein. Applicant requests that the reference in the IDS be made of record in the subject application.

Claims 15 and 22 have been rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Applicant notes that the issues raised in the Office Action pertain to antecedent basis issues that have been rendered moot via the amendments presented in this response. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Claims 1-12, 13, 15, 16 and 22-25 are rejected under 35 U.S.C. § 103(a) as obvious over Goldsborough (WO 00/75302, 2000) in view of Greene *et al.* (1999). The Office Action argues that Goldsborough teaches many of the aspects of the claimed invention with respect to the treatment of a sample for the protection of a nucleic acid and its subsequent isolation. The Office Action indicates that Goldsborough differs from the claimed invention in the use of primary amines for the deprotection of the nucleic acids. However, the Office Action cites Greene *et al.* for the proposition that it would have been obvious to one skilled in the art at the time the invention was made to use a primary amine (*e.g.*, ethylenediamine as taught in Greene *et al.*) for the removal of protecting groups on protected/stabilized nucleic acids because of the recognition of its use in the cleavage of esters. Applicant notes that the Office Action argues that the application specifically directs the artisan to the work of Greene *et al.* and that the artisan would have been substituting one known method of ester cleavage for another and that one skilled in the art would have had a reasonable expectation of

success in arriving at the claimed invention. Applicant respectfully disagrees and traverses this rejection.

With respect to the alleged direction to Greene *et al.* argued in the Office Action, Applicant presumes that the Office Action refers to the following passage (at page 6, paragraph 2): "Whilst many chemical deprotecting methods are also known for removing acetyl groups (Protecting Groups in Organic Synthesis, Greene and Wuts, 2nd Edition, Wiley Interscience) most if not all **involve either a base or acid, conditions that are likely to lead to extensive cleavage of the desired RNA during deprotection**" (emphasis added). As would be noted from this passage, the application specifically indicates that the methods disclosed in Greene *et al.* involve conditions that are likely to lead to extensive cleavage of the desired nucleic acid (*e.g.*, RNA) during deprotection. Thus, and contrary to the statements made in the Office Action, the as-filed application would not have directed one skilled in the art to the deprotection methods disclosed in Greene *et al.* as the expected result would have been degradation of the desired end product of the claimed methods (*i.e.*, undegraded nucleic acids). Applicant further submits that various compounds containing primary amines were recognized in the art to catalyze the cleavage of nucleic acids (Perreault and Anslyn, Angew. *Chem. Int. Ed. Engl.*, 1997, 36:432-450, see page 444).

As the Patent Office is aware, the U.S. Court of Appeals for the Federal Circuit "has previously found a proposed modification inappropriate for an obviousness inquiry when the modification rendered the prior art reference inoperable for its intended purpose." *In re Fritch,* 972 F.2d 1260, 1266 n.12, 23 USPQ2d 1780, 1783 n.12 (Fed. Cir. 1992) (citing *In re Gordon*, 733 F.2d 900, 902, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984)). In this case, Applicant respectfully submits that those skilled in the art, contrary to the assertions in the Office Action, would not have been motivated to substitute the art recognized methods for deprotection of nucleic acids for those taught in Greene *et al.* because the degradation of the nucleic acids, as opposed to its deprotection, would have been the expected result given the recognition and state of the art as discussed above. Accordingly, it is respectfully submitted that the cited combination of references fails to establish the *prima facie* obviousness of the claimed invention and reconsideration and withdrawal of the rejection is respectfully requested.

Claim 14 is rejected under 35 U.S.C. § 103(a) as obvious over Goldsborough (WO 00/75302, 2000), in view of Greene *et al.* and further in view of Padhye (U.S. Patent No. 5,808,041). The Office Action indicates that Goldsborough and Greene *et al.* do not teach the elution of nucleic acid using EGTA with a pH above 9; however, Padhye teaches elution in a sample containing EDTA or EGTA and further teaches elution of nucleic acids in buffers with a pH about 8.5. Claims 17-21 are rejected under 35 U.S.C. § 103(a) as obvious over Goldsborough (WO 00/75302, 2000), in view of Greene *et al.* and further in view of Michelsen *et al.* (U.S. Patent No. 6,355,792). The Office Action states that Michelsen *et al.* teach a method of isolating nucleic acids by their binding to silica gel or hydroxyapatite; teach eluting with a Tris containing buffer; teach the hydroxyapatite is treated with DNA/RNA mixture before washing; and teach pretreatment of hydroxyapatite with a phosphate containing compounds. Applicant respectfully traverses each of these rejections.

It is respectfully submitted that the claims are not obvious over the cited combination of Goldsborough, Greene *et al.* and Padhye or Michelsen *et al.* As noted above, one skilled in the art would not have been motivated to substitute the deprotection protocols of Greene *et al.* for those disclosed in Goldsborough (or recognized in the art) because the deprotection protocols of Greene *et al.* would have been expected to result in the degradation of the nucleic acids. Michelsen *et al.* and Padhye fail to remedy the defects noted in the cited combination of Goldsborough and Greene *et al.* As the Patent Office is aware, all the claim limitations must be taught or suggested by the prior art in order to establish the *prima facie* obviousness of a claimed invention (*CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) citing *In re Royka*, 490 F.2d 981, 985 (C.C.P.A. 1974)). As the cited combinations of references fail to teach or suggest all of the limitations of the claimed invention, it is respectfully submitted that the *prima facie* obviousness of the claimed invention has not been established and reconsideration and withdrawal of the rejections is respectfully requested.

Applicant also notes that the as-filed application contains a discussion of unexpected benefits arising from the use of primary amine containing compounds in the claimed methods. For example, the specification indicates, at page 8, "... primary amines can not only remove protecting groups from the 2'-OH position of RNA but also lead to only limited cleavage of the phosphodiester backbone of RNA as would be expected for a base. It was also unexpected that primary amines such as ethylenediamine and triethylenetetramine reduce the amount of protein contamination binding to

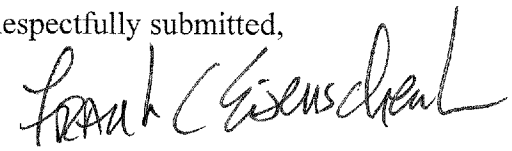
metal ions such as those present in hydroxylapatite." Further, the application indicates that the "[a]ddition of 200µl of ethylenediamine to a 1.45ml reaction containing 200µl of plasma, 50µl of 1-methylimidazole and 1.2ml of tetrahydrofuran / acetic anhydride (2 :1 vol :vol) has been found to reduce protein binding by 7.5 fold whilst not affecting RNA yield. This is an unexpected result because hydroxylapatite and silica surfaces are well known to bind proteins" (see page 12). As the Patent Office is aware, comparative data in the specification which is intended to illustrate the claimed invention must be considered in reaching a conclusion with regard to the obviousness of the claims. *In re Margolis*, 785 F.2d 1029, 228 U.S.P.Q. 940 (Fed. Cir. 1986). Accordingly, it is respectfully submitted that the claimed invention is not obvious in view of the cited combination of references and reconsideration and withdrawal of the rejection of record is respectfully requested.

Applicant believes that the pending claims are in condition for allowance and such action is respectfully requested.

Applicant invites the Examiner to call the undersigned if clarification is needed or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Respectfully submitted,



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